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ATTORNEY DOCKET No.: 2003946-0056 (ANDI/CIP)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Chiba, *et al.* Examiner: NYA  
Serial No.: 10/657,910 Art Unit: 1614  
Filing Date: September 9, 2003  
Title: MACROCYCLIC COMPOUNDS USEFUL AS PHARMACEUTICALS

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450  
Sir:

**TRANSMITTAL**

In regard to the above-referenced patent application, enclosed please find the following:

1. Information Disclosure Statement (6 pp.);
2. Form PTO-1449 (2 pp.);
3. Cited Art (21 References, excluding copies of U.S. Patents); and
4. Return-Receipt Postcard.

If any additional fees are required to be paid or if any overpayment has been made, please charge same to Deposit Account No. 03-1721.

Respectfully submitted,

  
Nadège M. Lagneau  
Registration No.: 51,908

Dated: July 12, 2004

PATENT GROUP  
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**Certificate of Mailing**

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July 12, 2004  
Date

  
Signature  
Kathy Hart Gagnon

Typed or Printed Name of person signing certificate



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Sir:

**STATEMENT**

Pursuant to the duty of disclosure under 37 C.F.R. §§1.56, 1.97 and 1.98, Applicant requests consideration of this Information Disclosure Statement.

**Type of Statement**

The present Information Disclosure Statement is:

- An *original* Information Disclosure Statement; or  
 A *supplemental* Information Disclosure Statement.

Compliance with 37 CFR § 1.97

The present Information Disclosure Statement is being filed:

- [ ] Pursuant to 37 CFR § 1.97(b); no fee or certification is required:
- [ ] Within three months of the filing date of a national application other than a continued prosecution application under § 1.53(d);
- [ ] Within three months of the date of entry of the national stage as set forth in § 1.491 in an international application;
- [X ] Before the mailing of a first Office action on the merits; or
- [ ] Before the mailing of a first Office action after the filing of a request for continued examination under § 1.114.
- [ ] Pursuant to 37 CFR § 1.97(c) after the dates listed above but before the mailing date of any of a final action under § 1.113, a notice of allowance under § 1.311, or an action that otherwise closes prosecution in the application; Applicant hereby *either*:
- [ ] Certifies that *either*:
- [ ] each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement; or
- [ ] That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making

reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement.; or

- [ ] Includes herewith the fee set forth in § 1.17(p).
- [ ] Pursuant to 37 CFR § 1.97(d), after the mailing date of any of a final action under § 1.113, a notice of allowance under § 1.311, or an action that otherwise closes prosecution in the application; Applicant hereby *both*:
  - [ ] Certifies that *either*:
    - [ ] each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement; or
    - [ ] That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement.; and

Content of the Information Disclosure Statement

Applicant hereby makes of record in the above-identified application the reference(s) listed on the attached form PTO-1449 (modified). The order of presentation of the references should not be construed as an indication of the importance of the references.

Applicant includes copies of references as indicated below:

- [X] A copy of each cited reference not indicated with a † is included;
- [ ] Copies of references indicated with an asterisk on the attached form PTO-1449 are not included pursuant to 37 CFR § 1.98(d) because they were previously provided to the United States Patent Office in an Information Disclosure Statement that complies with 37 CFR § 1.98(a)-(c) and was submitted in the following patent application that is relied upon in the present case for an earlier effective filing date under 35 USC § 120:

Serial Number	Filing Date	Status

- [ ] Copies of English translations of one or more non-English references are included.

Applicant hereby makes the following additional information of record in the above-identified application:

Applicant certifies that the Information Disclosure Statement *either*:

- [ ] Does not contain non-English language citations;
- [ X ] Does contain non-English language citations, of which an English language translation of the Abstract for each is provided herein:

Includes one or more translations of a non-English citation.

Remarks

The submission of this Information Disclosure Statement should not be construed as a representation that a search has been made.

The submission of this Information Disclosure Statement shall not be construed to be an admission that the information cited in the statement is, or is considered to be, material to patentability as defined in § 1.56(b) .

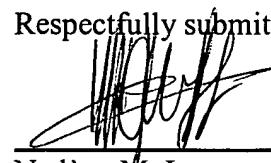
The submission of this Information Disclosure Statement shall not be construed as a representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. §102.

It is respectfully requested that:

1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;
2. The enclosed form PTO-1449 be signed by the Examiner to evidence that the cited patent(s) and publication(s) has (have) been fully considered by the Patent and Trademark Office during the examination of this application; and
3. The citations for the patent(s) and publication(s) be printed on any patent which issues from this application.

Notwithstanding any statements by Applicants, the Examiner is urged to form his or her own conclusions regarding the relevance of the cited reference(s).

Respectfully submitted,



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Nadège M. Lagneau, Ph.D.  
Reg. No. 51,908

PATENT GROUP  
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Tel: (617) 248-5000  
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Dated: July 12, 2004

Form PTO-1449  
(REV. 8-03)

U.S. Department of Commerce  
Patent and Trademark Office

Attorney Docket  
2003946-0056  
(ANDI/CIP)

In re Application No.  
Not Yet Assigned

INFORMATION

DISCLOSURE STATEMENT

(Use several sheets if necessary)

JUL 14 2004

O I P E  
S C I O F  
P A T E N T  
O F F I C E

Applicant: Chiba *et al*

Filing Date:  
September 9, 2003

Group:  
NYA

U.S. PATENT DOCUMENTS

Examiner's Initials	U.S. Patent No.	Applicant	Issue Date	Class	Subclass
	† 5,674,892	Giese, et al.	October 7, 1997	514	450
	† 5,727,726	Giese, et al	March 17, 1998	514	449
	† 5,795,910	Giese, et al.	August 18, 1998	514	450
	† 6,265,603 B1	Lewis, et al.	July 24, 2001	560	9

U.S. PATENT APPLICATIONS

Examiner's Initials:	Serial Number:	Applicant:	Filing Date:	Group:	Art Unit:

FOREIGN PATENT DOCUMENTS

Examiner's Initials'	Document No.	Country	International Publication Date	Translation	
				Yes	No
	EP 0 606 044 A1	EP	November 29, 1993		
	GB 2 323 845 A	UK	October 7, 1998		
	JP 8- 40893	JP	February 13, 1996		X
	WO 96/13259	PCT	May 9, 1996		
	WO 00/38674	PCT	July 6, 2000		
	WO 00/39314	PCT	July 6, 2000		
	WO 01/36003 A2	PCT	May 25, 2001		
	WO 02/48136 A1	PCT	June 20, 2002		X

OTHER DOCUMENTS

Examiner's Initials	Citation (Including Author, Title, Date, Pertinent Pages, Etc.)
	Copy of International Search Report for PCT/US03/07377.
	Agatsuma, et al., " Revised Structure and Stereochemistry of Hypothemycin", <i>Chem.Pharm.Bull.</i> ; 41(2): 373-375 1993.
	Chen, et al., "Activation of p38 MAP kinase and ERK are required for ultraviolet-B induced c-fos gene expression in human keratinocytes", <i>Oncogene</i> , 18: 7649-7476, 1999.
	Dombrowski, et al., "Production of a Family of Kinase-inhibiting Lactones from Fungal Fermentations", <i>J. Antibiot.</i> , 52(12): 1077-1085, 1999.

† Copies of references not included – requirement waived pursuant to USPTO OG Notice of 8/5/03

**INFORMATION  
DISCLOSURE STATEMENT**  
*(Use several sheets if necessary)*

Applicant: Chiba *et al*Filing Date:  
September 9, 2003      Group:  
NYA

Ellestad, et al., "New Zearalenone Related Macrolides and Isocoumarins from an Unidentified Fungus", *J. Org. Chem.*, **43**(12):2339-2343, 1978.

Li, et al., "Rays and arrays: the transcriptional program in the response of human epidermal keratinocytes to UVB illumination", *The FASEB Journal*, Article 10.1096/fj.01-0172fje, published online September 17, 2001.

Kastelic, et al., "Induction of Rapid IL=1 $\beta$  mRNA Degradation in THP-1 Cells Mediated Through the AU-Rich Region in the 3'UTR by a Radicicol Analogue", *Cytokine* **8**(10): 751-761, 1996.

Matsuoka, et al., "Inhibition of HgCl<sub>2</sub>-induced mitogen-activated protein kinase activation by LL-Z1640-2 in CCRF-CEM cells", *Eur. J. Pharmacol.*, **409**(2): 155-158, 2000.

Rawlins, et al., "Inhibition of endotoxin-induced TNF- $\alpha$  production in macrophages by 5Z-7-oxo-zeaenol and other fungal resorcylic acid lactones", *Int. J. Immunopharmacol.*, **21**(12): 799-814, 1999.

Tak, et al., "NF- $\kappa$ B-a key role in inflammatory diseases", *J. Clin. Investigation*, **107**(1): 7-11, 2001.

Takehana, et al., "A radicicol-Related Macroyclic Nonaketide Compound, Antibiotic LL-Z1640-2, Inhibits theJNK/p38 Pathways in Signal-Specific Manner", *Biochem. Biophys. Res. Commun.*, **257**(1): 19-23, 1999.

Tatsuta, et al., "The First Total Synthesis of a Macroyclic Anti-protozoan, LL-Z1640-2", *Chem. Lett.*, **Vol. 2**, 172-173, 2001.

Yamamoto, et al., "Therapeutic potential of inhibitionof the NF- $\kappa$ B pathway in the treatment of inflammation and cancer", *J. Clin. Investigation*, **107**(2), 135-142, 2001.

## EXAMINER

## DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

† Copies of references not included – requirement waived pursuant to USPTO OG Notice of 8/5/03